

REMARKS

Claims 1, 2, 4, 5, 9-18, and 42-61 are pending. By this amendment, claims 3, 6-8, and 27 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue these canceled claims in a divisional or continuation application(s).

The amendments to the claims do not introduce new matter. Accordingly, Applicants respectfully request entry of these amendments.

Claim Rejections under 35 U.S.C. §103(a) in view of Yamazaki and Ness

On pages 2-4, the Office Action rejects claim 1, 2, 4-5, 9-16, 42-50, 52, 54, and 56-58 under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,699,719 (hereinafter “Yamazaki”) in view of U.S. Patent No. 6,150,103 (hereinafter “Ness”). Applicants respectfully traverse the rejection.

Applicants respectfully submit that Yamazaki and Ness do not teach or suggest each and every element of claims 1, 42, and 49. Claim 1 recites “said surface comprises a coating of an amine-presenting molecule, and said biological membranes are deposited directly to said coating.” Claims 42 and 49 recite “said surface comprises a coating of an amine-presenting molecule, and each of said biological membrane microspots comprises a biological membrane directly deposited to said coating.”

Yamazaki neither teaches nor suggests the use of biological membranes directly deposited to a coating of amine-presenting molecules. Yamazaki describes the fabrication of arrays of fluid bilayer membranes, but the bilayer membranes employed in Yamazaki are separated from the supporting surface by “an aqueous film of corresponding thickness.” *See* column 8, lines 1-11. This aqueous film can be made of “a buffered saline solution (e.g., PBS)” and can be “readily changed (taking care, of course, to keep the supported bilayer submerged at all times) by, e.g., flow-through rinsing with a solution having a different composition.” *See* column 10, lines 4-9. Accordingly, Applicants respectfully submit that Yamazaki fails to teach or suggest the use of biological membranes that are directly deposited to a coating of amine-presenting molecules.

The combination with Ness does not remedy this deficiency. Ness describes an array of biomolecules in which the biomolecules are positioned throughout a polyethyleneimine layer overlying a substrate of the array. The biomolecules employed in Ness, however, are not biological membranes. Biomolecules, even with large sizes or molecular weights, are structurally and functionally different from biological membranes. Accordingly, Ness, as

with primary reference, Yamazaki, fails to teach or suggest the use of biological membranes that are deposited to a coating of amine-presenting molecules.

Because Yamazaki and Ness neither disclose nor suggest each and every element of claims 1, 42, and 49, Applicants respectfully submit that Yamazaki and Ness do not render these claims obvious. *See* MPEP §2143.03 (“To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art”).

For the similar reasons, Applicants respectfully submit that Yamazaki and Ness, either individually or in combination, also fail to teach or suggest the elements of claim 57. Claim 57 recites “a plurality of biological membranes directly deposited to a coating on a surface of said array” and “said coating comprises an amine-presenting molecule or a silane.” As noted above, the bilayer membrane employed in Yamazaki is separated from the supporting surface by an aqueous film and, therefore, is not deposited directly to a coating of amine-presenting or silane molecules. Ness likewise does not teach or suggest the use of biological membranes. Accordingly, Yamazaki and Ness do not teach or suggest all of the elements of claim 57 and, therefore, do not render claim 57 obvious.

In addition, Applicants respectfully submit that Yamazaki implicitly teaches away from the methods recited in claims 1, 42, 49, and 52. In particular, Yamazaki describes that a thin polymer film (e.g., polyacrylamide or dextran) can be deposited to an array surface to form bilayer-compatible regions and that this thin polymer film can be coupled to the array surface by 3-methacryl-oxypropyl-trimethoxy-silane. *See* column 18, lines 20-29. By not depositing bilayer membranes directly to 3-methacryl-oxypropyl-trimethoxy-silane, Yamazaki implicitly teaches that direct deposition of bilayers to silane is undesirable. Accordingly, Applicants respectfully submit that Yamazaki implicitly teaches away from the techniques set forth in the present invention, particularly the methods recited in claims 1, 42, 49, and 52.

Applicants also respectfully submit that the Office Action has failed to establish any motivation to combine Yamazaki and Ness. The Federal Circuit has repeatedly emphasized that evidence of a motivation to combine must accompany a challenge based on multiple references. *See In re Dembiczak*, 175 F.3d 994 (Fed. Cir. 1999) and *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534 (Fed. Cir. 1998). *See also* MPEP §2143.01 (The prior art must suggest the desirability of the claimed invention). As the Federal Circuit observed, the “case law makes clear that the best defense against the subtle but power attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching

or motivation to combine prior art references.” *See In re Dembiczak*, 175 F.3d 994, 998, 999 (Fed. Cir. 1999).

On page 3, the Office Action contends that “it would have been obvious to one of ordinary skill in the art for the support to have a layer of PEI in the method of Yamazaki et al to bind biomolecules such as bilayer membranes, as Ness et al suggests that PEI is effective in binding biomolecules due to its hydrophilicity, and the fact that PEI contains many amino groups for forming salts with acidic groups in biomolecules.” However, Applicants respectfully submit that a mere statement that combination of the prior art to meet the claimed invention would have been within the ordinary skill in the art is not alone sufficient to establish a prima facie case of obviousness. *See* MPEP §2143.01 (emphasis added). Accordingly, Applicants respectfully request the Examiner to provide documentary proof to substantiate the alleged motivation to combine Yamazaki and Ness. Moreover, as noted above, Yamazaki contemplates the use of a thin polymer film which is coupled to the array surface by 3-methacryl-oxypentyl-trimethoxy-silane. By not using 3-methacryl-oxypentyl-trimethoxy-silane for membrane deposition, Applicants respectfully submit that Yamazaki implicitly teaches away from the use of silane and other functionally similar molecules, such as PEI, for membrane deposition.

On page 8, the Office Action further contends that “the motivation is that PEI is very effective in the capacity of binding biomolecules due to its hydrophilicity, and the fact that PEI contains many amino groups which can form salts with acidic groups in a biomolecule.” However, this alleged motivation is very different from a motivation to deposit biological membranes to a PEI coating for assessing the interactions between membranes and ligands or toxins. In fact, it is un-expected prior to the present invention that a substantial portion of membranes deposited to a silane or amine coating would resist desorption and exhibit desired lateral fluidity. *See* paragraph 41 on page 12 of the present application. These properties enable a meaningful assessment of the interactions between deposited biological membranes and ligands or toxins. Neither Yamazaki nor Ness suggests this advantage, and Applicants need more guidance from the Examiner on the alleged motivation to combine. *See In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000) (“Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed”) (emphasis added). *See also In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998) (“In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with

no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed") (emphasis added).

Based on all of the above reasons, Applicants respectfully submit that the Office Action has failed to establish *prima facie* obviousness of claims 1, 42, 49, and 57. Reconsideration and withdrawal of the §103(a) rejections of these claims are, therefore, respectfully requested.

Because claims 2, 4-5, 9-16 and 18 depend from claim 1, claims 43-48 and 54 depend from claim 42, claims 50 and 56 depend from claim 49, and claim 58 depends from claim 57, Applicants respectfully submit that claims 2, 4-5, 16, 18, 43-48, 50, 54, 56 and 58 are also patentable over Yamazaki in view of Ness at least for the reasons set forth hereinabove. Reconsideration and withdrawal of the §103(a) rejections of these claims are also respectfully requested.

Claim Rejections under 35 U.S.C. §103(a) in view of Yamazaki, Ness and Pluskal

On pages 4-5, the Office Action rejects claim 17 as being obvious over Yamazaki in view of Ness, as applied above, and in further view of U.S. Patent No. 5,004,543 to Pluskal et al. (hereinafter "Pluskal"). Applicants respectfully traverse the rejection.

Claim 17 depends from claim 1. As discussed above, Applicants respectfully submit that Yamazaki and Ness neither disclose nor suggest the invention of claim 1. Accordingly, Yamazaki and Ness do not teach or suggest each and every element of claim 17.

The proposed combination with the tertiary reference Pluskal does not remedy this deficiency. Pluskal relates to a hydrophobic material having a crosslinked, cationic charge-modifying coating such that the majority of the ion exchange capacity of the material is provided by fixed formal positive charge groups. Pluskal does not describe any biological membrane deposited to a coating of amine-presenting molecules. Accordingly, Pluskal is outside the purview of the present invention, particularly claim 17.

Because Yamazaki, Ness and Pluskal, either individually or in combination, do not teach or suggest the elements of claim 17, Applicants respectfully submit that these references do not render claim 17 obvious. *See* MPEP §2143.03 ("To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art").

Applicants also respectfully submit that the Office Action has failed to establish any motivation to combine Yamazaki, Ness and Pluskal. The Federal Circuit has repeatedly

emphasized that evidence of a motivation to combine must accompany a challenge based on multiple references. See In re Dembiczak, ATD Corp. v. Lydall, Inc., and the MPEP, as cited and quoted hereinabove.

On page 5, the Office Action contends that “it would have been obvious to one of ordinary skill in the art to have a charge-modified, hydrophobic microporous membrane as the support in the method of Yamazaki et al and Ness et al, as suggested by Pluskal et al, as the membrane is highly effective for macromolecular adsorption applications under a variety of conditions.” However, Applicants again respectfully submit that a mere statement that combination of the prior art to meet the claimed invention would have been within the ordinary skill in the art is not alone sufficient to establish a *prima facie* case of obviousness. See MPEP §2143.01 (emphasis added). Accordingly, Applicants respectfully request the Examiner to provide some form of documentary proof to substantiate the alleged motivation to combine the disparate references Yamazaki, Ness and Pluskal.

Based on all of the above reasons, Applicants respectfully submit that the Office Action has failed to establish *prima facie* obviousness of claim 17. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the §103(a) rejection of claim 17.

Claim Rejections under 35 U.S.C. §103(a) in view of Yamazaki and Nova

On pages 5-7, the Office Action rejects claims 1, 2, 4-5, 9-16, 18, 42-51, 53, 55, and 57-61 as being obvious over Yamazaki, as applied above, in view of U.S. Patent No. 5,741,462 to Nova et al. (hereinafter “Nova”). Applicants respectfully traverse the rejection.

Applicants respectfully submit that Yamazaki and Nova, either alone or in combination, fail to teach or suggest each and every element of claims 1, 42, 49, and 57. As discussed above, Yamazaki neither teaches nor suggests the use of biological membranes deposited to a coating of amine-presenting or silane molecules. Nova relates to matrix materials with remotely addressable or remotely programmable recording devices that contain data storage units. Nova describes that a data storage device with memory can be coated with a polymer, which is then treated to contain an appropriate reactive moiety or, in some cases, the device may be obtained commercially already containing the reactive moiety, and may thereby serve as the matrix support upon which molecules or biological particles are linked. See column 15, lines 13-18. Nova also describes that the reactive moieties can be “amino silane linkages, hydroxyl linkages or carboxysilane linkages.” See column 15, lines

19-20. However, Nova does not teach or suggest using these reactive moieties for the deposition of biological membranes for the assessment of interactions between membranes and ligands or toxins, as set forth in the presently-claimed invention. Accordingly, Applicants respectfully submit that Nova neither discloses nor suggests the elements of claims 1, 42, 49, and 57.

Because Yamazaki and Nova, either individually or in combination, do not teach or suggest the invention of claims 1, 42, 49, and 57, Applicants respectfully submit that these references do not render claim 17 obvious. *See* MPEP §2143.03 (“To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art”).

Furthermore, Applicants respectfully submit that the Office Action has failed to establish any motivation to combine Yamazaki and Nova. Specifically, Applicants respectfully submit that Yamazaki and Nova do not teach or suggest that deposition of a biological membrane to a coating of amine-presenting or silane molecules would maintain the membrane’s lateral fluidity. In fact, Applicants respectfully submit that it is un-expected, prior to the present invention, that a substantial portion of membranes deposited to a silane or amine coating would resist desorption and exhibit desired lateral fluidity. *See* paragraph 41 on page 12 of the present application. Neither Yamazaki nor Nova discloses or suggests this advantage. Accordingly, Applicants respectfully submit that the Office Action has failed to identify any motivation to make a biological membrane deposited to a coating of amine-presenting or silane molecules. *See In re Kotzab* and *In re Rouffet*, as cited and quoted hereinabove.

In addition, as noted above, Applicants respectfully submit that Yamazaki implicitly teaches away from the present invention.

On page 6, the Office Action contends that it would have been obvious to one of ordinary skill in the art to treat an array with γ -aminopropylsilane or carboxysilanes in the method of Yamazaki, as suggested by Nova, in order to obtain an appropriate reactive moiety to link molecules or biological particles. However, as noted, a mere statement that combination of the prior art to meet the claimed invention would have been within the ordinary skill in the art is not alone sufficient to establish a *prima facie* case of obviousness. *See* MPEP §2143.01 (emphasis added). *See also* MPEP §2143.01 (The prior art must suggest the desirability of the claimed invention). As the Federal Circuit observed, the “case law makes clear that the best defense against the subtle but power attraction of a hindsight-based

obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references.” See In re Dembiczak. See also In re Kotzab and In re Rouffet, as cited and quoted hereinabove.

Based on all of the above reasons, Applicants respectfully submit that the Office Action has failed to identify any motivation to combine Yamazaki and Nova and, therefore, failed to establish *prima facie* obviousness of claims 1, 42, 49, and 57. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the §103(a) rejections of these claims.

Because claims 2, 4-5, 9-16, 18 and 51 depend from claim 1, claims 43-48 and 53 depend from claim 42, claims 50 and 55 depend from claim 49, and claims 58-61 depend from claim 57, Applicants respectfully submit that these claims are also patentable over Yamazaki in view of Nova at least for the reasons set forth above. Accordingly, reconsideration and withdrawal of the §103(a) rejections of these claims are also respectfully requested.

Claim Rejections under 35 U.S.C. §103(a) in view of Yamazaki, Nova and Pluskal

Finally, on pages 7-8, the Office Action rejects claim 17 as being obvious over Yamazaki in view of Nova and Pluskal, all as applied above. Applicants respectfully traverse the rejection.

Claim 17 depends from claim 1. As discussed above, Yamazaki, Nova and Pluskal, do not teach or suggest each and every element of claim 1. Accordingly, Applicants respectfully submit that these references neither disclose nor suggest the elements of claim 17. Therefore, Applicants respectfully submit that Yamazaki, Nova and Pluska do not render claim 17 obvious. See MPEP §2143.03 (“To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art”).

Applicants also respectfully submit that the Office Action has failed to establish any motivation to combine Yamazaki, Nova and Pluskal. The Federal Circuit has repeatedly emphasized that evidence of a motivation to combine must accompany a challenge based on multiple references to avoid hindsight analyses. See In re Dembiczak, ATD Corp. v. Lydall, Inc., 159 and the MPEP, as cited and quoted hereinabove.

On page 8, the Office Action contends that “it would have been obvious to one of ordinary skill in the art to have a charge-modified, hydrophobic microporous membrane as the support in the method of Yamazaki et al and Nova et al, as suggested by Pluskal et al, as

the membrane is highly effective for macromolecular adsorption applications under a variety of conditions.” However, a general statement that combination of the prior art to meet the claimed invention would have been within the ordinary skill in the art is not alone sufficient to establish a prima facie case of obviousness. See MPEP §2143.01 (emphasis added). Accordingly, Applicants respectfully request the Examiner to provide some form of documentary proof to substantiate the alleged motivation to combine Yamazaki, Ness and Pluskal.

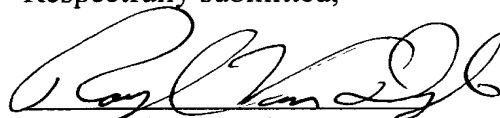
Based on all of the above reasons, Applicants respectfully request the Examiner to reconsider and withdraw the §103(a) rejection of claim 17.

CONCLUSION

Applicants respectfully submit that this application is in condition for allowance. Favorable consideration and prompt allowance of the claims are earnestly solicited. Although Applicants believe that no fee is due for the instant response, the Commissioner is hereby authorized to charge any payment deficiency to deposit account number 19-2380 referring to attorney docket number 015275-060007.

Should the Examiner believe that anything further is desired in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants’ attorney of record.

Respectfully submitted,



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